VOL. XXI. April, 1896. No. 4.

THE
Journal
OF
Nervous and Mental Disease.

Original Articles.

THE SPINAL CORD IN PERNICIOUS ANÆMIA.[1]

By JAMES HENDRIE LLOYD, AM., M.D.

Neurologist to the Philadelphia Hospital; Physician to the Methodist Episcopal Hospital, and to the Home for Crippled Children.

THE recognition of the involvement of the spinal cord in pernicious anæmia is apparently quite recent. Lichtheim, in 1887, was one of the earliest observers, if not the earliest, to write on this subject. According to Bowman,[2] he laid stress upon the special character of the changes found in the cord, as distinguishing these cases from tabes. This distinction is apparently being lost sight of by some writers, for it is becoming rather the fashion to speak of pernicious anæmia being complicated with locomotor ataxia.

It should be borne in mind that cases of pernicious anæmia with involvement of the spinal cord are neither clinically nor anatomically identical with locomotor ataxia. It is true that some of them resemble tabes more than others, but even those that resemble tabes most are not identical with it. On the other hand, some of these cases are quite distinct from tabes, and have been placed by some writers in a separate class as presenting a type somewhat similar to disseminated sclerosis.

Minnich,[3] in 1892, published a paper based upon six cases, and illustrated with diagrams of the changes in the cord. In his paper it is quite evident that these cases varied considerably in type. The symptoms in some cases resembled tabes; in some, disseminated sclerosis. Progressive weakness was marked in all cases, whereas ataxia was seen in only one-half of the number. Loss of the knee-jerks was seen in only two cases, in only one of which was there the Argyll-Robertson pupil. In only two cases were there subjective sensory changes, while anæsthesia, though frequently observed, was not seen in all. Loss of control of the sphincters was seen in one-half of these cases toward the end. In these six cases of Minnich's the anatomical findings, as shown in the diagrams, varied as well as the clinical phenomena; they all showed a wonderful uniformity, however, in the changes found in the posterior columns. These changes were found in Goll's columns, extending across into Burdach's columns, but invariably leaving a line of normal white tissue along the edge of the posterior horn. In most cases, also, the degeneration did not extend forward to the gray commissure. The root-zone almost always escaped. The variations in Minnich's cases were in the areas involved; the posterior columns were invariably involved, as just described, but in some cases the process stopped, or almost stopped there, while in others the type was rather that of a more disseminated process, involving (especially in Case V.) the direct and crossed pyramidal tracts. There was no shrinking in the posterior columns, as is seen in tabes.

---

[1] This paper appears also in the "Philadelphia Hospital Reports," vol. iii. 1896.

[2] *Brain*, Summer Number, 1894, p. 198.

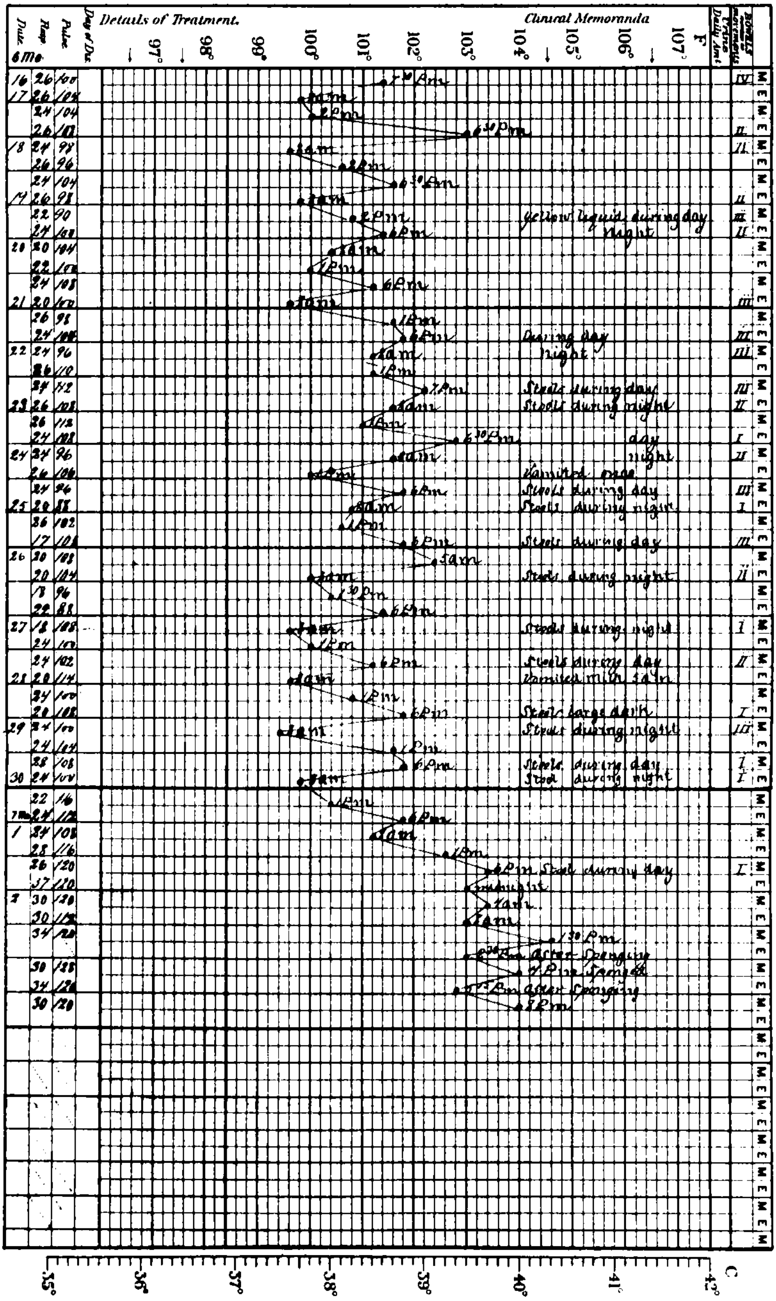
[3] Zeitschrift für klin. Med., vol. xxi., 1892.

Other cases published since Minnich's—notably, Bowman's and Burr's—have adhered to this peculiar type of posterior sclerosis, the root-zone and Lissauer's tract escaping. Bowman's case, however, presented also degeneration of the crossed and direct pyramidal tracts.

Bowman describes the earlier process as a swelling of the medullary sheath (to three or four times the diameter of a healthy fibre). The swollen sheath does not take the Weigert stain readily. The axis-cylinder appears normal. This description of Bowman's accords closely with what I have observed in a recent case, before I had read his paper. I have described and depicted these changes in the following pages.

The history of the case is as follows:

S. C., thirty-seven years, white, male, machinist, single, born in Ohio.



Temperature Chart in a Case of Pernicious Anaemia.

Family History.—Father suffered much from malaria, and died of apoplexy at sixty-four years of age. Mother and one sister died from a chronic diarrhœa similar to the one that the patient has at present. One sister died of some abdominal tumor complicated with diabetes mellitus.

Personal History—The patient in boyhood suffered from malaria in his home on the Ohio river, but he has never had a recurrence since he moved to Philadelphia twenty years ago. In July, 1893, he had what he describes as a severe attack of gastro-enteritis, from which he never completely recovered, the diarrhœa persisting until his admission into the hospital. He has had typhoid fever twice. He had "inflammation of the bowels"[4] when nineteen years old. He has been a hard drinker, and gives a history of syphilis of fifteen years' standing.

He is a machinist, but he gives no history of exposure to lead of any kind. For the past two years he has been unable to work on account of increasing weakness. He has consulted many physicians and attended dispensaries without relief.

Throughout this period he has experienced cold sensations running up and down his legs, also "prickings" in the same regions, and a feeling as if he were "walking on cotton." He has had, he says, "loss of power" in his legs, but he does not give any history of ataxia in his gait; he has always moved as well in the dark as in the light. He has had girdle sensations about the abdomen. There have never been any subjective eye-symptoms, nor involvement of the rectum or bladder.

On the patient's admission, May 1, 1894, it was noted that the knee-jerks were normal. Ankle-clonus was absent. Sensation was normal. The man was very weak and could not walk straight. At this time he was already markedly anæmic. The lips were colorless, the skin a peculiar lemon-white hue, and the fat of the body fairly well preserved. After his admission it was noted that he was subject to attacks of suddenly occurring localized œdema, affecting first his legs and ankles, and then suddenly leaving them and affecting his face.

The patient complained of pain in his abdomen, centering around the umbilicus, worse after a stool.

---

[4] Appendicitis? The patient had marks of wet cups over the lower abdominal walls.

The diarrhœa was rather irregular; at times profuse, with a large number of liquid stools in succession, followed by an interval of from six hours to several days, during which the bowels were not disturbed. He occasionally passed a little blood in his stools. He had no hemorrhoids nor history of them. He never coughed nor had any subjective pulmonary symptoms.

Examination, June 16, 1894.—The patient's skin is of a lemon yellow color. Subcutaneous fat is fairly well preserved, and general nutrition is good. The conjunctivæ are very pale and of a pearly-yellow white, and are thrown into folds when the eyes are rolled, as the finger is pressed against them. Knee-jerks are about normal. Ankle-clonus is absent. The gait is that of a very weak person, but it is not truly ataxic. The pupils are equal; they respond to light and accommodation. Speech is normal. The tests for sensation are not satisfactory, as the man apparently cannot fix his attention. Sensation, however, is apparently not markedly impaired. The mental processes seem to be dull and confused, and to be growing worse, but are probably not disturbed more than can be explained by the patient's anæmic condition.

Chest.—Apex beat, in the fifth interspace, one-half inch inside the nipple line, is slightly diffused. Cardiac dulness is increased to the right, extending to the right border of the sternum. At the apex a rough systolic murmur is heard transmitted to the axilla. In the tricuspid area a softer blowing murmur is heard over the xyphoid cartilage. No murmurs are detected in the aortic or pulmonary areas. There is marked pulsation in the suprasternal notch and in the vessels of the neck. Loud venous hums are heard on both sides over the jugulars. The pulse is rapid (100–115), rather full, soft and easily compressible. The respiratory sounds are rather weak, but nothing abnormal is detected in the lungs.

Abdomen.—The liver is about normal in size. The spleen is somewhat, but not markedly, enlarged. At present the patient is having from four to six stools in the twenty four hours, watery and light yellow. Under the microscope a few pus-cells, a very few cells resembling red blood cells, and granular matter, are found in the stools. Rectal examination gives negative results.

Blood.—Red cells=1,280,000. Hæmoglobin, 23 per cent. Macrocytes, microcytes, and many poikylocytes, with some nucleated red cells, are shown. (See Fig. 1.)

Urine.—Amber in color; specific gravity, 1020; acid. Chemical and microscopical examinations reveal nothing abnormal.

June 23, 1894.—The blood was examined by Dr. Daland to-day. He reported as follows: "The blood as it emerged from the puncture was pink in color. Its consistency and coagulability were lessened. The hæmatokrit showed 16 per cent. (800,000 to c.mm.) of red cells, and slight excess of white cells. The red cells were of good color. Many poikylocytes with characteristic pear and flask shapes were seen. The leukocytes seemed a trifle increased in number, perhaps 12,000 to 15,000. The smaller-sized leukocytes predominated in number; many were about the same size as the red cells, and rarely was a large white cell visible. The white cells seemed filled with coarsely granular material. Some were irregular in shape, and occasionally one was seen to throw out pseudopods." Count of white cells (3040 to c.mm.).

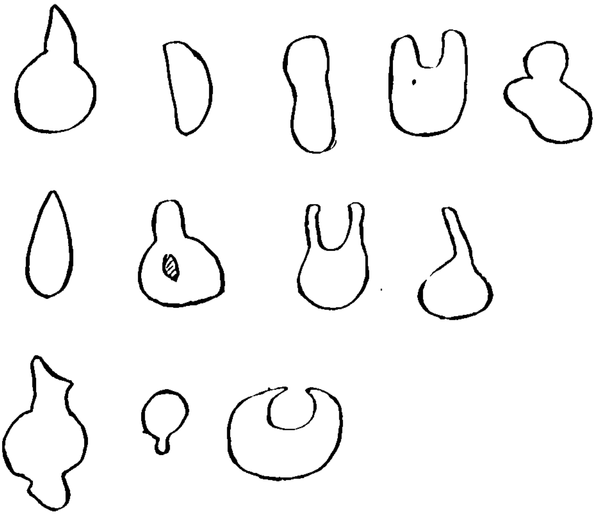


FIG. 1.—Forms of Poikylocytes noted in the Blood.

June 24.—An examination of the eyes was made today by Dr. de Schweinitz, who found the vessels of both retinas diminished in size and the retinas the seats of many hemorrhages.

July 1.—Red cells=648,000 to c.mm.

July 2.—Spots of extravasated blood have appeared at the base of the sacrum. The patient is much weaker. Cerebral anæmia is very marked. Carphologia has been present at intervals for the past week.

July 3.—Death at 6 A. M.

Post-Mortem Notes. July 4, 1894, thirty hours after death.—Body of fairly nourished man. Skin of lemon-yellow color. Subcutaneous fat is well preserved and of an orange color. It measures three-quarters of an inch in thickness in the abdominal wall. Tissues seem practically bloodless, and the muscles are highly colored. No œdema of tissues is noted. The marrow of the laminæ of the vertebræ is soft, but not fluid; it is dark-red in color. The abdominal cavity does not contain fluid.

The appendix is adherent at the tip, as if it might have been the seat of an old inflammation, but does not show signs of any recent disturbance.

The liver seems slightly diminished in size, extending barely to the costal margin, is yellow on section, and appears fatty.

The spleen measures 6x4x3 inches. Capsule is somewhat thickened and wrinkled. There are four notches on the edge of the organ, giving it a serrated appearance. On section the tissue is dark and soft, and the pulp is rather easily squeezed out.

The kidneys, on section, appear to be fatty. The cortex is about the usual thickness.

The pancreas is normal.

Intestines.—No enlargement of the mesenteric glands is notable. No marks of ulcers; no tubercles nor tumor.

DESCRIPTION OF SECTIONS.—*Stains.*—(1) Carminate of ammonia; (2) Hæmatoxylon; (3) Methyl-green; (4) Weigert; (5) Biondi-Heidenhein.[5]

POSTERIOR COLUMNS.—*Dorsal Region.*—The degeneration does not occupy the whole of the posterior columns. In the dorsal region the area of degeneration is about midway between the posterior median septum on either side, and the posterior horn of the same side; hence it involves part of each postero-median and postero-external column. (Columns of Goll and Burdach.)

---

[5] Cervical region not removed with cord.

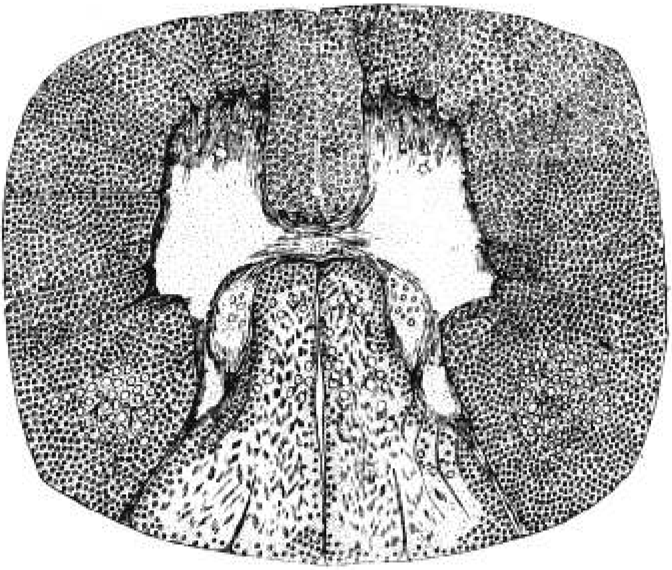


FIG. 2.—The Spinal Cord in Pernicious Anæmia. Dorsal Region.

This area does not extend forward quite to the posterior gray commissure, the normal white matter with the cut ends of the nerve-fibres being conspicuous around the anterior edge of the degenerated area. Around the post-median septum the degeneration is not so dense as at a slight distance away from it on either side. At the point of deepest degeneration no normal tissue can be traced; *i. e.*, no nerve-fibres are visible. Hence the area of deepest degeneration may be described as spread around the division line between the columns of Goll and Burdach on either side, and not extending quite to the posterior commissure in front, nor quite to the periphery of the cord behind. The posterior root-zone is not seriously involved in this cord—a fact which accords with the clinical findings of no ataxia and of preserved knee jerks. Still these trunks do not escape entirely, the most median ones being involved toward the periphery, before they emerge from the cord.

Lumbar Region.—Almost, if not quite, normal in the posterior columns.

LATERAL COLUMNS.—The lateral columns have been studied very carefully. In the dorsal region, as shown

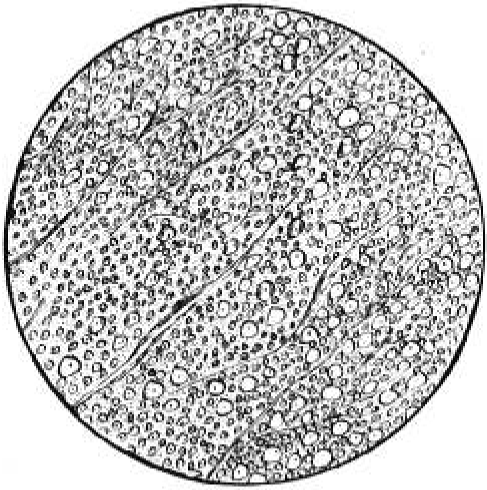


FIG. 3.—The Spinal Cord in Pernicious Anæmia. From the Lateral Columns, showing swollen Nerve-fibres.

especially in the section stained with methyl-green, it is evident that some change has occurred in them. This is shown (1) by an increase in the neuroglia, and (2) by great distension of some of the nerve-tubules. In some of these distended tubules the axis-cylinder can still be seen; in others, not. This distension of the nerve-tubules, it seems to me, is of great significance. It probably shows an early stage of degeneration, in which some irritant is acting upon, or even infiltrating into, the tissues. In the first stage the tubule swells; then the axis cylinder breaks and finally shrivels; and, finally, the neuroglia, which has been proliferating all the while, begins to contract and blot or squeeze out the true nerve tissue. In this cord the early stage is probably seen, in which the most conspicuous feature is the swelling of the nerve-tubules. In the lumbar region, where, of course, the lateral columns are not so large as in the dorsal cord, these columns are not nearly so markedly involved. These swollen tubules may also be seen in some of the degenerated tissue in the posterior columns.

Deiter's cells show with unusual clearness in the posterior columns in some regions. They can be picked out especially well with the carmine stains.

The membranes are not distinctly involved in this cord.

The anterior horns, with their multipolar cells, are normal in both dorsal and lumbar region. The cells are conspicuously free from disease in all the sections.

Nerve-trunks.—These cannot be said to be markedly affected so far as the shape and contour, and the amount of interstitial tissue is concerned. With the Weigert stain, however, the fibres do not stain evenly, and this may possibly be an indication of commencing change in them.

Concluding Remarks.—The anatomical changes, just depicted, explain why these cases of pernicious anæmia do not present the identical symptoms of locomotor ataxia. As in Minnich's and in Bowman's cases, already referred to, the posterior root-zones are but partially involved. It cannot be said, however, that they escape entirely in my case. It is possible that the degree of their involvement varies slightly in different cases, and this variation may explain the absence or presence of such tabetic symptoms as the loss of the knee-jerks, the ataxia and the subjective sensory symptoms. In some cases, in which the disease-process is more disseminated, and the lateral tracts involved, the patients present the clinical picture of ataxic paraplegia. It is probable that this would have been the case with my patient had he lived longer, as the lateral tracts were becoming distinctly involved, and must soon have become sclerosed.

It seems almost useless in a purely clinical and anatomical study to speculate about the essential cause of pernicious anæmia and the relation of this cause to the changes in the spinal cord. Other writers, who have essayed to do this, have not succeeded in throwing any light upon this important subject. It is a purely pathological question, and cannot be solved apparently by ordinary bedside methods or by post-mortem histological studies. It may be permissible here, however, to call attention to a few points and to a few analogies, which may assist the future investigator.

First, it is to be noted that this patient's range of temperature is strongly indicative, according to received opinions, of some irritant or toxic substance circulating in the blood. It was continuously high for weeks before death; for at least two weeks before the end it did not come down to the normal once. It rose steadily toward the end, registering once almost as high as 105°. When it is considered that the autopsy revealed nothing in any organ or tissue that could account for such continuous high range of temperature, the conclusion seems almost forced that it could be explained only by an abnormal blood state produced by some toxine.

Second, the character of the tissue-change in the spinal cord is strongly suggestive of the action of a poison. The change begins apparently in the parenchyma; thus, as we have seen, the myeline sheath becomes enormously swollen, and this apparently before the neuroglia begins to proliferate markedly. It may be too much to assume positively that this parenchymatous change is always the result of the action of a toxic substance, yet it is certainly in harmony with what we know already of the action of some such substances. In this connection, it will be interesting to note in the future whether the spinal cord is ever involved in a similar way in the ordinary secondary anæmias.

Finally, the persistent diarrhœa, sometimes with hemorrhage, may have some special significance in this case. Especial care was observed at the autopsy in examining the gastro-intestinal tract, but nothing was observed that could, in any way, account for the symptom.

Acknowledgments are due to Dr. J. Dutton Steele, resident physician, for clinical work done in this case.